

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

**(19) World Intellectual Property Organization**  
International Bureau



**(43) International Publication Date  
29 July 2004 (29.07.2004)**

PCT

(10) International Publication Number  
**WO 2004/062710 A2**

**(51) International Patent Classification<sup>7</sup>:**

A61M

**(71) Applicants and**

**Inventors:** BRUGGER, James [US/US]; 4 Savory Street, Newburyport, MA 01950 (US). BURBANK, Jeffrey [US/US]; 18 Sunrise Road, Boxford, MA 10920 (US). GREEN, Brian [US/US]; 14 Lakeside Terrace, Westfield, MA 01886 (US).

PCT/US2004/000476

**(22) International Filing Date:** 7 January 2004 (07.01.2004)

**(25) Filing Language:** English

**(26) Publication Language:** English

**(30) Priority Data:** 60/438,567 7 January 2003 (07.01.2003) US

(71) **Applicant** (for all designated States except US):  
**NXSTAGE MEDICAL INC.** [US/US]; 439 South Union Street, 5th Floor, Lawrence, MA 01843 (US).

**(71) Applicants and**

(72) **Inventors:** BRUGGER, James [US/US]; 4 Savory Street, Newburyport, MA 01950 (US). BURBANK, Jeffrey [US/US]; 18 Sunrise Road, Boxford, MA 10920 (US). GREEN, Brian [US/US]; 14 Lakeside Terrace, Westfield, MA 01886 (US).

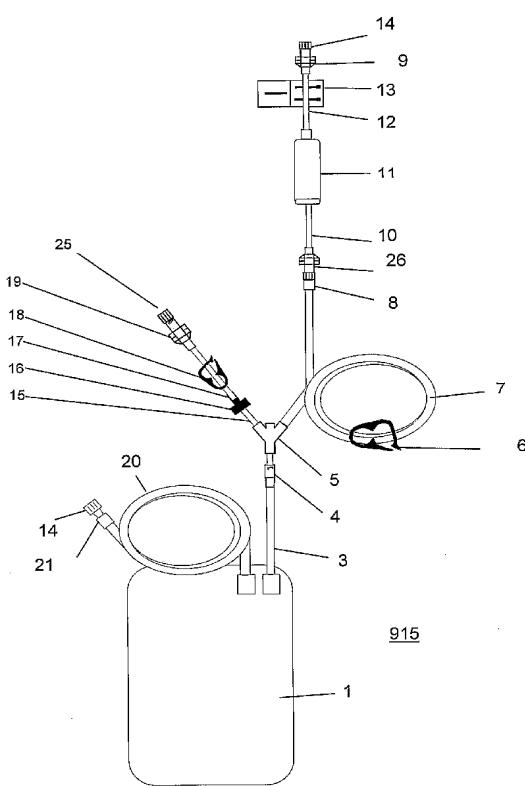
(74) **Agent:** CATAN, Mark; Proskauer Rose LLP, 1585 Broadway, 5th Floor, New York, NY 10036 (US).

(81) **Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

[Continued on next page]

**(54) Title:** BATCH FILTRATION SYSTEM FOR PREPARATION OF STERILE REPLACEMENT FLUID FOR RENAL THERAPY

**(57) Abstract:** A method and device for blood treatment involving infusion of replacement fluid are provided. In an embodiment, fluid is passed either by pump or passively by gravity feed, through a microporous sterilization filter from a fluid source to a replacement fluid container. The latter forms a batch that may be used during treatment. The advantage of forming the batch before treatment is that the rate of filtering needn't match the rate of consumption during treatment. As a result, the sterilization filter can have a small capacity. In another embodiment, a filter is placed immediately prior to the point at which replacement fluid is injected into the patient's bloodstream. The latter may be used in combination with the former embodiment as a last-chance guarantee of sterility and/or that the fluid is free of air bubbles. It may also be used as the primary means of sterile-filtration.





(84) **Designated States** (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished upon receipt of that report

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

BATCH FILTRATION SYSTEM FOR PREPARATION OF STERILE  
REPLACEMENT FLUID FOR RENAL THERAPY

Background of the Invention

5 During hemofiltration, hemodialysis, hemodiafiltration, ultrafiltration, and other forms of renal replacement therapy, blood is drawn from a patient, passed through a filter, and returned to the patient. Depending on the type of treatment, fluids and electrolytes are exchanged in the filter between a dialysate and/or extracted from the blood by filtration. One effect may be a net loss of fluid and electrolytes  
10 from the patient and/or exhaustion of dialysate, with a concomitant need for its replenishment, again depending on the type of treatment. To replace fluid lost from the patient and keep the patient from dehydrating, replacement fluid may be injected into the patient at a rate that matches a rate of loss, with an adjustment for a desired net change in the patient's fluid complement. To replace exhausted dialysate, fresh  
15 dialysate is continuously circulated through the filter.

Conventionally, dialysate and/or replacement fluid is supplied from either of two sources: batches of fluid, typically in multiple bags, or a continuous source of water that is sterile-filtered and added to concentrated electrolytes to achieve the required dilution level. Because replacement fluid is injected directly into the patient, replacement fluid must be sterile. When either method is used to generate replacement fluid, there is a risk of contamination of the fluid. Contamination may occur, for example, at the point where bags of fluid are accessed ("spiked") or at any connection in the fluid circuit linking the source to the patient.

In many instances, such therapies may require a large quantity of  
25 sterile fluid. A typical way to provide the large quantity of replacement fluid is to

provide multiple bags of replacement fluid, dialysate, or infusate. The connection of these bags of fluid to an extracorporeal blood circuit, there is a risk of touch-contamination resulting in the introduction of biological contaminants into the fluids.

Presently, methods of producing large volumes of dialysate from tap water are known, but each requires complex water purification and standardization equipment, since impurities and cleaning additives such as chlorine vary greatly in tap water from municipality to municipality and within a municipality over time. (See Twardowski U.S. Patent Nos. 6,146,536 and 6,132,616.) Moreover, dialysate solution, whether prepared online or prepackaged, while of the proper concentration for use as a sterile replacement fluid, never enters the patient's body. Instead, dialysate flows past a semipermeable membrane that permits ions to be exchanged across the membrane until a balance between their concentrations in blood and their concentrations in the dialysis is achieved. This is effective to remove impurities from the blood and to add missing electrolytes to the blood. Because it does not have to be infused, dialysate is less expensive than solutions prepared as replacement fluids, which are injected directly into a patient.

Attempts to render dialysate sufficiently sterile for use as a replacement fluid in hemofiltration and hemodiafiltration have focused on continuous sterilization processes that require a separate dialysate filtration / purification apparatus that must be periodically purged and verified to provide sufficient constant flow of sterile replacement fluid required for hemofiltration. (See Chavallet U.S Patent Nos. 6,039,877 and 5,702,597.) Such devices are necessarily complicated and require separate pumping systems for the sterilization process. In addition, the rate of supply of dialysate for such systems is very high, requiring an expensive filter to be

used. The same high-rate problem exists for the generation of replacement fluid for hemofiltration, and therefore also requires an expensive filter.

#### Summary of the Invention

5           In the present invention, sterile replacement fluid or dialysate may be generated in batch form by sterile-filtering. According to embodiments of inventions disclosed, non-sterile fluid is passed through a filter prior to treatment to prepare a batch of replacement fluid. This process may be permitted to take any length of time because the rate of flow of non-sterile replacement fluid (or components thereof) 10          through the filter is completely independent of the rate of consumption by the renal therapy. Because the filters used for sterile-filtering tend to be expensive, it may be desirable for such a batch process to employ a small filter for such filtration. Such a filter can have a flow capacity that is much lower than that required for real-time 15          filtering of the replacement fluid (or components). In addition to preparation of sterile fluid from non-sterile fluid, embodiments of inventions disclosed may be used to sterilize already-sterile fluid as a precaution against touch contamination.

Generally replacement fluid is heated before being infused into a patient. This is often accomplished by heating the fluid as it is being infused with a heater with sufficient heating capacity. The capacity of the heater must be matched to 20          the mass flow of the fluid and the temperature rise required. In a batch preparation process, where a batch of fluid is prepared over a substantial period before use, a small heater may heat the replacement fluid over a long period of time. Insulation may be provided to prevent heat loss. An insulating outer container for the sterile replacement fluid may be provided. For example, the container may be an insulated

box with room for one or more large disposable sterile bags of the type normally used for infusible fluids.

The preparation of warm sterile replacement fluid may be automated by a control process that permits a user to set up the fluids and other materials well in advance of a scheduled treatment. The process would ensure that the replacement fluid is sterilized and heated to the proper temperature when the treatment is to begin. The automation process may permit the user to select how far in advance of the treatment the preparation should be performed. This may be useful, for example, where a particular source of replacement fluid has proved to release more than a usual quantity of dissolved gases upon heating. Heating the replacement fluid and permitting it to settle for a time before it is used may allow gases to come out of solution and settle at the top of the batch vessel or vessels. The automation process may be incorporated in the control functions of renal therapy machine.

The invention or inventions will be described in connection with certain preferred embodiments, with reference to the following illustrative figures so that it may be more fully understood. With reference to the figures, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention or inventions only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention or inventions. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention or inventions, the description taken with the drawings making apparent

to those skilled in the art how the several forms of the invention or inventions may be embodied in practice.

Brief Description of the Drawings

5 Fig. 1 is a schematic illustration of a standalone/retrofit apparatus system for batch filtration of a sterile replacement fluid.

Fig. 2 is a flow chart illustrating an exemplary control procedure applicable to various embodiments of the invention including those of Figs. 1 and 3.

10 Fig. 3 is a schematic illustration of a blood treatment machine with an attached subsystem for batch preparation of sterile replacement fluid.

Figs. 4A and 4B are illustrations of fluid filters that may be used in various embodiments of the invention.

Fig. 5 illustrates an exemplary blood treatment system with a filter used to sterilize and/or degas replacement fluid during treatment.

15 Figs. 6-8 illustrate a blood treatment machine and cartridge providing various supporting mechanical features for the embodiment of Fig. 5 and further embodiments, including one in which a quality of replacement fluid is sensed before infusion.

20 Fig. 9 illustrates a disposable fluid circuit kit which may support various embodiments of the invention.

Fig. 10 illustrates a set up for priming a blood treatment process, which components of the invention may be used to support.

Fig. 11 illustrates a portion of a blood treatment machine that allows a pump used as part of the blood treatment to also be used to control the filtering of fluid to provide a batch of infusible replacement fluid.

Fig. 12 illustrates replacement fluid container tubing set.

5 Fig. 13 illustrates a replacement fluid preparation apparatus.

Figs. 14, 15, and 16 illustrate portions of the replacement fluid preparation apparatus of Fig. 13.

#### Detailed Description

10 Referring to Fig. 1, a filter 160 filters fluid from a source of fluid 150 to generate a batch of sterile replacement fluid 130. The filter 160 may be, and preferably is, a microporous filter that blocks all materials except dissolved electrolytes and water. Thus, the result of the filtration process is to sterilize the raw fluid from the source of fluid 150. The source of fluid 150 may be a container of 15 sterile or non-sterile replacement fluid, one or more containers of constituents which, when combined, form a proper replacement fluid. Any of the latter may include a continuous source such as a water tap. One or more conduit elements form a line 120 to convey the source fluid 150 through the filter 160 and into a batch container 147. The latter may be any type of sterile, preferably disposable container, for example, a 20 large IV bag. It may also include a number of such containers appropriately interconnected to permit flow into and out of them in the fashion of container 147.

Included in the conveyance from source fluid 150 to sterile replacement fluid 130 may be a pump 190, such as a peristaltic pump. The pressure at an outlet of the filter 160 may be sensed by a pressure sensor 162 and the pump 190

controlled by a controller 170 to insure a predefined transmembrane pressure (TMP) threshold of the filter 160 is not breached. The TMP may be maintained at a maximum safe level to maximize throughput. Note that complexity may be avoided if the source fluid 150 is arranged such as to maintain a desired TMP at the filter 160  
5 without the need of a pump 190 or pressure sensor 162. For example, the source fluid 150 may be provided by a batch container elevated at a certain height to provide a desired head. Note that a control valve 165 or a speed of the pump 190 may be used to regulate the flow rate to maintain desired TMP limits.

A control/shutoff valve 180 may provide the controller 170 the ability  
10 to stop the flow of fluid through the filter 160 once a desired volume is reached. A heater 185 may be provided to warm the sterile replacement fluid 130 to prepare it for use. An insulated container 145 may be used to reduce heat loss so that heater 185 can be a relatively low power type. The heater 185 may be controlled by the controller 170 to ensure the replacement fluid 130 is at a desired temperature when  
15 required to be used. Alternatively the heater 185 can be controlled by an independent device actuated by, for example, a pressure sensor (not shown) triggered by the flow of fluid into the batch container 147, a timer (not shown) settable to trigger based on a predefined treatment time, or some other means. Preferably, in either case, a temperature regulator (e.g., a temperature sensor 183 combined with logic in  
controller 170) regulates power to the heater to ensure a required temperature is  
20 maintained and not exceeded. The temperature sensor 183 may be used to sense the quantity of sterile replacement fluid by the rate of detected temperature increase versus heater output. The temperature sensor 183, heater 185, and sterile replacement fluid 130 can be modeled in any desired fashion. For example one may neglect all but

the thermal mass of the RF, assume perfect heat transfer (including assuming the RF fluid to be isothermal). Then, the mass would be given by the product of the temperature change, the thermal capacitance of the fluid, and the heat output rate of the heater. More complex theoretical or empirical algorithms would be a simple 5 matter to derive and implement. Once the mass of fluid is calculated to be below a certain level, the controller 170 may be programmed to respond in accord with the assumption the sterile RF is exhausted. Equivalently, the controller 170 may simply respond to some predefined rate of temperature rise of the temperature sensor 183.

When the temperature of the sterile replacement fluid 130 is raised, 10 dissolved gas may come out of solution. This may cause bubbles to accumulate inside the replacement fluid container 247, which is undesirable because of the risk of infusing bubbles into the patient's bloodstream. To help ameliorate that problem, a vibrator or ultrasonic transducer may be provided 183 to cause bubbles to coalesce and rise to a top of the container 147. As a result, bubble-free replacement fluid may 15 be drawn through the outlet 148.

A connector 195 may be provided for connecting the source fluid to the line 120. The connector may be a luer, spike, threaded adapter, or any other suitable type. Although the various controls indicated above are shown to be controlled an automatic controller 170, each may be controlled also by manual 20 mechanisms.

The Fig. 1 embodiment allows replacement fluid to be prepared in batch for later use. Thus, the rate of filtration of replacement fluid need not match the requirements of the treatment process or preparatory steps such as priming. As a result, a low capacity filter may be used for the filter 160. For example, typically only

a small quantity of expensive media is required to make a small-capacity filter and as such, the cost of a low capacity filter can be much smaller than a high capacity filter. Also, other features found in high capacity filters, such as a large ratio of media surface to volume of the filter module are achievable only by means of folding or 5 forming media into shapes that can be difficult to manufacture, such as tubes. Thus, savings can be achieved in simplification of the configuration of the filter as well. Relatively small filters with simple planar media held in plastic casings are available and suitable for this purpose.

The configuration of Fig. 1 may be retrofitted for use with an existing 10 treatment system. For this purpose, the outlet 148 may provide with any required connection adapter. A user interface 175 for entering data into the controller 170 may be provided as well.

Referring now to Fig. 2, a control algorithm for controlling the heater 185, pump 190, valves 165/180, etc. begins with the a setting of a time for treatment 15 S10, for example by entering a time into the controller 170 via a user interface (UI) 175. The time can be entered manually or automatically by means of, for example, a data signal from a remote source via a switched or network circuit. The time for treatment may be obtained from a treatment calendar entered into the controller 170, which also may be obtained from a remote source. In the present simple algorithm, 20 first and second time intervals T1 and T2 are defined representing the interval required for filtration of RF and the interval required for heating of RF, respectively. These values may be obtained from any of the above means (e.g., local manual or remote entry via UI/interface 175) or from data encoded on one of the consumables involved in the process. For example, the filter 160, the RF fluid container 147, the

source fluid 150 container(s), or any other consumable may be provided with one or more bar-codes, RFID tags, or other suitable encoding device. Such devices may provide values for T1 and T2, tables of values that depend upon other factors, or other data from which T1 and T2 may be derived.

5           The controller 170 waits until it is time to start the flow of raw RF fluid from source fluid 150 toward container 147 by comparing a current time (indicated by a clock internal to the controller 170, which is not shown) to a difference between a scheduled treatment time and T1, which represents the lead time (ahead of the scheduled treatment) required for the filtering process. A loop through  
10          step S20 is exited to step S30 when the clock reaches the treatment time minus T1. At step S30, the flow of source fluid 150 through the filter 160 is initiated. If the pump 190 is present, it may be started and regulated according to a specified TMP. The latter may be provided to the controller 170 manually or automatically through UI/interface 175. Automatic entry may be by way of a data store such as bar-code or  
15          RFID attached to the filter, for example which may be read when the filter 160 is installed in a chassis with a corresponding reader device (not shown). Note, as mentioned above, the source fluid may be sterile and the filtration process provided as a guarantee against contamination, for example by accidental touching.

Once the flow of source fluid 150 is initiated, the controller waits for  
20          the required time for applying power to the heater 185. The delay and the initiation are controlled by step S40 which is exited to step S50 only when the treatment time minus the predefined interval T2 is reached. As mentioned above, alternatively, the heater may be triggered by detecting fluid such as by means of a sensor (not shown) triggered by the presence of sterile replacement fluid 130 in the container 147. The

sensor may be any of a variety of types, such as an ultrasonic sensor, capacitance sensor, mass sensor, optical sensor, etc.

Once the heater is started, the controller 170 may wait for the source fluid to be exhausted at step S60. Step S60 exits to step S70 when the source fluid is determined to be exhausted. The latter may be detected by integrating the flow rate to measure the total volume (the rate may be determined by the pumping rate, for example, or by a flow meter (not shown)). The exhaustion of the source fluid 150 may also be indicated by a quantity indicator (e.g., a level indicator) in the sterile replacement fluid container 147 or an intermediate container supplied through a drip chamber, for example. Alternatively, the exhaustion of the source fluid 150, if supplied from a fixed-volume container, may be indicated by a sensor such as an ultrasonic sensor, capacitance sensor, mass sensor, optical sensor, a scale, etc. Yet another alternative is to sense gas or a precipitous rise in negative pressure (sensed by a pressure sensor which is not shown) at the pump 190 inlet. At step S70, the line 120 may be clamped by actuating shutoff/control valve 180. Additionally, if appropriate, the pump 190 may be deactivated at the point where the exhaustion of the source fluid 150 is detected at step S70.

According to an embodiment, as the fluid is pumped, the TMP of the filter, as indicated by pressure sensors 162, may be monitored. If the TMP is determined by the controller 170 to be, at any point, below a predetermined nominal value or to have changed precipitously during filtration, the controller 170 may trigger an alarm or take some other action to insure that the resulting replacement fluid is handled appropriately. For example, a back-up filter could be added during treatment as discussed with respect to Fig. 5. The TMP results could trigger an alarm at any

point during filtration or could be assessed and reported at step S70, before treatment would begin.

The controller 170 pauses again at step S80 to wait for the sterile fluid to be exhausted. This may be indicated by a signal from the treatment machine (e.g., 5 received via UI/interface 175) or by direct measurement by a sensor, such as an ultrasonic sensor, capacitance sensor, mass sensor, optical sensor, a scale, etc. As mentioned above, the controller 170, or the heater 185 itself, may be provided with a threshold temperature-rise rate that indicates the mass of fluid in the replacement fluid container 147 has fallen below a minimum level. The loop of step S80 is exited to 10 step S90 where power to the heater 185 is terminated.

Note that all the functionality attributed to the controller 170 may be provided, via a control interface, by a controller (not shown) internal to a treatment machine. For example, the apparatus of Fig. 1 could be provided as an optional module for such a treatment machine rather than a retrofit module.

15 Referring now to Fig. 3, a combination blood treatment system and sterile replacement fluid device 310 has a replacement fluid preparation subsystem 305 configured substantially as the device of Fig. 1. A filter 260 filters fluid from a source of fluid 250 to generate a batch of sterile replacement fluid 230 as in the embodiment of Fig. 1. Again, the source of fluid 150 may be a container of sterile or 20 non-sterile replacement fluid, one or more containers of constituents which, when combined, form a proper replacement fluid and any of the latter may include a continuous source such as a water tap. A line 220 conveys the source fluid 250 through the filter 260 and into a batch container 247, which may be any type of sterile, preferably disposable container, for example, a large IV bag. It may also

include a number of such containers appropriately interconnected to permit flow into and out of them in the fashion of container 247.

Again, a pump 290 may be provided and pressure at an outlet of the filter 260 may be sensed by a pressure sensor 262. The pump 290 may be controlled 5 by a controller 270 to insure a maximum safe TMP to maximize throughput. Again, the pump 290 is not required and the source fluid 150 may be arranged such as to maintain a desired TMP at the filter 160 without the need of the pump 290 or pressure sensor 262 by elevation. A control valve 265 or a speed of the pump 290 may be used to regulate the flow rate to maintain desired TMP limits.

10 A control/shutoff valve 280 may provide the controller 270 the ability to stop the flow of fluid through the filter 260 once a desired volume is reached. A heater 285 may be provided to warm the sterile replacement fluid 130 to prepare it for use. An insulated container 245 may be used and the heater controlled as discussed with respect to the Fig. 1 embodiment. Bubbles may be controlled, as discussed 15 above, by means of a vibration or ultrasonic transducer 230 as discussed above with regard to the previous embodiment.

A connector 295 may be provided for connecting the source fluid to the line 220. The connector may be a luer, spike, threaded adapter, or any other suitable type. Although the various controls indicated above are shown to be 20 controlled an automatic controller 270, each may be controlled also by manual mechanisms. Other aspects of the control mechanisms for the embodiment of Fig. 3 may be provided as discussed with respect to Figs. 1 and 2.

The benefits of the Fig. 2 embodiment are similar to those of the Fig. 1 embodiment in that it allows replacement fluid over a time period that is not driven by

the speed of supply to the treatment process. As a result, a low capacity filter may be used for the filter 260 with the attendant benefits identified above. Note that the UI/interface 275 and controller 270 are shared in the present embodiment by the treatment machine. Thus, any information required for control of both the treatment 5 and preparation of sterile replacement fluid 230 would not need to be communicated to a separate controller such as controller 170. Note also that the communications among the illustrated components is provided by a channel 202 which may be wire harness, separate wires, a bus, a wireless channel or any suitable communications/power transmission device.

10 In the embodiment of Fig. 3, a predicted quantity of replacement fluid may be filtered and stored for use during treatment. If, however, for some reason, more is required, the treatment machine controller 270 could be configured to identify that situation and control the subsystem 305 components to provide it. Many blood treatment process employ a filter 220 to filter blood and into which replacement fluid 15 is supplied to a patient 225. More details on preferred embodiments of the treatment machine are discussed below.

In either of the above embodiments, the rate of flow of fluid during preparation of the batch of replacement fluid may be substantially less than the rate of consumption during treatment. In an exemplary embodiment of an application for 20 hemofiltration, the amount of replacement fluid consumed is between 9 and 18 l. and the rate of consumption is approximately 200 ml./min. Also, the media used for sterile filtration may be any suitable media that insures the quality of the replacement fluid is as desired. In the embodiments discussed above, it was assumed that the end sought was preparation of sterile replacement fluid employed microfiltration to

prevent the passage of pathogens. However, the invention could be used with other types of filtration or treatment processes to produce a batch of fluid consumed by a medical treatment process, for example, dialysate for hemodialysis treatment. The benefits accrue in particular when the time scale of preparation may be longer than the 5 time scale of consumption. Moreover, the benefits are more appreciable when some sort of energy-consuming process is required, such as heating, before consumption. Here, not only is the time scale of preparation compatible with a small inexpensive filter, but the long time scale permits heating of the replacement fluid over a long interval. To support this benefit, the batch container may be insulated to minimize 10 heat loss so a small heater will be adequate. Also, the preferred application for the present invention is in the context of hemofiltration because the quantity of fluid required for such treatment is relatively small.

Note that other motivations for filtering the fluid, in addition to or as an alternative to sterilization of a non-sterile fluid, is (1) removal of air bubbles and/or 15 (2) as a safety net for ensuring against accidental contamination. If bubble removal is the only concern, a drip chamber may be used instead of a filter. For removing bubbles, the filter preferably is of a type that permits the passage of fluid, but which blocks the passage of bubbles, for example due to its media pore size and the surface tension of the fluid.

20 Referring now to Fig. 4A, a preferred type of filter for some of the present embodiments has an inlet port 415 providing an inlet channel 410 communicating with an inlet chamber 440. An outlet leading port 405 provides an outlet channel 420 communicating with an outlet chamber 445. A piece of filter media 425 separates the inlet and outlet chambers 440 and 445. The fluid to be

sterilized enters the inlet chamber 440, is sterilized by passing through the filter media 425, and exits via the outlet chamber 445. A gas relief gasket 425 allows gas accumulating in the inlet chamber 440 to be released to the ambient atmosphere.

Internal supports and structural details are not shown in the illustration for clarity, but 5 a practical embodiment of the filter of Fig. 4 may have ribs for strength and internal supports for the media 425 and gasket 425 so that the filter 400 may be capable of tolerating a substantial TMP.

The gas relief gasket 425 may be of a porous hydrophobic material such as PTFE. Air bubbles trapped in the inlet chamber 440 can coalesce in the inlet 10 chamber 440 and exit via the air relief gasket 425. It may be, depending on the type of gas relief gasket 425 used, that a substantial TMP will be required to eliminate air.

An alternative to the gas relief gasket 425 is a gas relief valve 426 as shown in Fig. 4B. Since the inlet chamber 440 is connected to the non-sterile side of the filtration system, there is little risk of contamination if microbes were to enter 15 through a mechanical device such as the gas relief valve 426. The latter is illustrated figuratively and allows only gas to escape. Other features of the embodiment of Fig. 4B are labeled with the same numerals as features of the embodiment of Fig. 4A where they serve substantially identical functions and, thus, their descriptions are not repeated here.

20 Referring now to Fig. 5, the filters of Figs. 4A and 4B may be used for filtration of replacement fluid in the embodiment of Fig. 5 as discussed presently. Replacement fluid 360, which may or may not be sterile, is supplied to a hemofiltration machine 490. A replacement fluid pump 360 pumps the replacement fluid into a balancing mechanism 330 which meters the replacement fluid before it is

introduced, via a junction 485, into the venous (return) line 480 and ultimately into the blood stream of a patient 225. Waste fluid is drawn through a waste line 470 from a filter 395 and pumped via a waste pump 365 through the fluid balancing mechanism 330. The fluid balancing mechanism 330 meters the replacement fluid to match the 5 rate of withdrawal of waste fluid so that the patient's fluid balance is maintained during treatment. Actually, the rate of withdrawal of waste fluid may be less than the rate of metering of replacement fluid by pumping waste fluid through a bypass pump called an ultrafiltration pump 339. The latter sends some of the waste fluid directly to a waste fluid sump 380, thereby bypassing the fluid balancing mechanism 330. The fluid balancing mechanism is depicted figuratively and may operate in accord with 10 any suitable control device. Preferably it meters replacement fluid on an equal-volume or equal-mass basis. A preferred mechanism is described in US Patent Application No. 09/513,911, filed 2/25/00, entitled: "Synchronized Volumetric Fluid Balancing Systems and Methods," which is hereby incorporated by reference as if 15 fully set forth in its entirety herein. Various sensors and line clamps, indicated figuratively at 335, 355, 320, 385, and 390, may be provided to control flow and ensure safe operation.

A filter 337, is provided in the replacement fluid line 338 just upstream of the junction 485. The filter 337 may serve as a last chance safety net for ensuring 20 that replacement fluid is sterile and/or that all bubbles are removed before flowing into the venous line 480. To ensure that air is not infused into the patient's body, an air sensor 390 is often provided in hemofiltration systems, but detection of air normally triggers an alarm, automatic shutdown, and skilled intervention to restart the hemofiltration treatment. Obviously, this is undesirable so the system should, as

effectively as possible, insure that air or other gas is not injected into the venous line  
480.

Although in the embodiment of Fig. 5, a hemofiltration machine was  
discussed, other types of treatment processes may be provided a last-chance filter  
5 similar to filter 337. For example, hemodiafiltration, hemodialysis, or other  
treatments may require the infusion of replacement fluid and thereby benefit from a  
filter such as filter 337. Preferably, the filter 337 is substantially as in the  
embodiment of Fig. 4A. Thus, the filter 337 removes both air and pathogens.

Instead of employing a filter at the location indicated at 337, a drip  
10 chamber may be used. Suitable drip chambers are currently available with air vents  
and microfilters effective to remove pathogens, so they may be substituted for the  
filter 337. Also, in some cases, it may be that there is very little risk that the  
replacement fluid is contaminated with pathogens, the filter 337 may serve as a  
mechanism for removing only air or other gases. In such cases, drip chambers which  
15 remove gas (either with or without a vent), could be employed at the above location in  
the fluid circuit.

Referring now to Figs. 6, 7, and 8 the last chance filter or drip chamber  
(or combination device) 510 may be installed in a cartridge 520 that holds and orients  
blood and fluid circuits for a hemofiltration machine 540. In the embodiment shown,  
20 which is described substantially in US Patent Application No. 09/513,773 filed  
2/25/00 and entitled: "Fluid Processing Systems and Methods Using Extracorporeal  
Fluid Flow Panels Oriented Within A Cartridge," hereby incorporated by reference in  
its entirety as if fully set forth herein, fluid circuit components may be held in a  
cartridge 520 and clamped (as shown in Fig. 8 with the machine closing as illustrated

by the arrow 665) within a receiving gap 530 in a blood treatment machine such as hemofiltration machine 540. The cartridge 520 may have a preferred orientation which may insure a correct orientation for the last chance filter or drip chamber (or combination device) 510 if required by the particular device chosen. To insure 5 orientation of the last chance filter or drip chamber (or combination device) 510, the latter is preferably held by the cartridge 520 in a fixed orientation with respect to the cartridge 520.

In an alternative embodiment, the last chance filter or drip chamber (or combination device) 520 may be accompanied by a device 660 for measuring the 10 quality of the replacement fluid, such as conductivity or density. This may provide a last-chance check that the replacement fluid is of the correct type. For example, where such fluids are derived from mixtures, if the proportion is not exactly what is required, infusion could be harmful to the patient 225. An example of a device 660 to test the fluid could be a wettable pair of contacts (not shown) formed in a tubing set 15 650 of the cartridge may be used in conjunction with a resistance measurement device to measure the ion concentration of the fluid. Alternatively, a non-wettable sensor, such as an ultrasonic conductivity cell could be used. Other kinds of fluid quality sensors could be employed such as new types of specific-molecule detectors built on silicon wafers.

20 Preferably, the tubing set 650 and cartridge 620 of which it is a part form a disposable component that is used for one treatment and disposed of. Note that the fluid quality sensor 660 may be used alone or together with the last chance filter or drip chamber (or combination device) 510. Note, although figures 6 and 7 are detailed, they are intended to show various components figuratively and do not reveal

the details of the routing necessary to achieve the flow paths discussed with respect to them or as illustrated elsewhere.

Referring now also to Fig. 9, the tubing set and cartridge assembly 610, discussed previously, may incorporate the batch replacement fluid container 625 as part of a sterile replaceable set 690. The filter 615 may have a tube 622 with a connector 620 for attachment to a source fluid 250. A tube 635 may connect the filter to the batch replacement fluid container 625, which may be fitted with another tube 630 to convey fluid to the tubing set and cartridge assembly 610. Referring now also to Fig. 10, the batch replacement fluid container 625 may also be fitted with additional connectors 670 and/or extensions (not shown) to permit the batch replacement fluid container to be used for priming blood, replacement fluid, and/or waste lines. For example, as discussed in US Patent Application No. 09/905,246, filed 7/12/01, entitled: "Devices and Methods For Sterile Filtering of Dialysate," which is hereby incorporated by reference as if fully set forth in its entirety herein, replacement fluid is circulated through a replacement fluid container 740 to flush air out of all the fluid circuiting (not all shown) of a blood treatment apparatus 710. As described in detail in the '246 application incorporated by reference above, the venous (return) and arterial (supply) blood lines 725 and 730 may be temporarily connected via connectors 750 to the replacement fluid container 740 and fluid circulated through the container 740 until gas bubbles are substantially purged from the relevant circuits. Note, the replacement fluid container 740 corresponds to the containers 147 (Fig. 1), 247 (Fig. 3), and 625 (Fig. 9) in the foregoing figures and to respective containers in the application incorporated by reference immediately above. The air and other gases may settle in the replacement fluid container 740 as the fluid circulates. Liberation of

the gases would ordinarily be promoted by the application of heat from a heater 775  
(with power source 770), which may be employed as discussed with regard to the  
embodiments of Figs. 1-3 or in any suitable way to bring the temperature of the  
replacement fluid to body temperature. Replacement fluid circuits including line 735,  
5 blood circuits including lines 725 and 730, and waste fluid circuits including line 780  
may all be flushed with fluid from the container 740. The details of the blood  
treatment apparatus and its internal plumbing can vary. Replacement fluid may be  
transferred from the replacement fluid line 735 or from the blood line 735 to the waste  
line, for example through a filter, to flush the waste portion of the circuit including the  
10 waste line 780. Replacement fluid may circulate through the blood circuit including  
lines 725 and 730 as indicated to flush the blood circuit, at least a portion of which  
may be closed as indicated by the arterial and venous lines 730 and 735.

Disposable components, such as the circuit sets of Figs. 8 and 9 or the  
batch replacement fluid container 625 alone, or other components that may be used  
15 with the embodiments disclosed may be packaged with instructions for preparing  
infusible replacement fluid. For example, the source fluid 150/1250 or a concentrate  
which may be mixed to make the same (Figs. 1 and 3) may be supplied with  
instructions for sterile filtering the fluid as described in the instant specification. Such  
instructions may constitute packages of consumables or reusable components.

20 Note that benefits of the filtering method and apparatus discussed  
above may best be achieved by performing the filtration just prior to treatment,  
although this is not required. The filtering method may be performed at the treatment  
site. For example, non-sterile concentrate may be stored at the residence of a patient.  
The concentrate may be diluted with distilled water in a source fluid container (e.g.,

196 of Fig. 1) at the residence and processed as discussed in the instant application.

Because the infusible fluid is generated at the treatment site, the need for regulatory-

cleared fluids, such as might be obtained from a manufacturer, is not avoided. Cost

savings and storage-space economies can thus be realized by the patient. This is

5 particularly important in view of the fact that renal replacement therapies are often

administered many times per week and storage and cost of consumables can present a

serious problem in a residence or any other facility.

Referring now to Fig. 11, a blood treatment machine, a portion of

which is illustrated figuratively at 810, may permit a pump 845 that, during treatment,

10 conveys replacement fluid to a patient, to be used for filtering a sterile filtering a non-

sterile source fluid. Here, the machine 810 has a common guide 850 that

accommodates a fluid line 815 through which fluid is conveyed by the pump 845, for

example a peristaltic pump. During treatment, the line 815-825 may be guided by a

first selected guide 830 in a first direction toward other components of an internal

15 fluid circuit (not shown) as indicated at 825. During sterile-filtering, fluid may be

pumped by the same pump 845 through a line 815-820 that is allowed to pass out of

the blood treatment machine 810 via a different guide 835. This allows the line 815-

820 to be fed to an external connection to the sterile fluid container (not shown) as

indicated at 820.

20 Referring now to Fig. 12, another embodiment of a replacement fluid

container portion of a disposable tubing set includes a replacement fluid container 1,

a break-off female luer lock connector 4, a y-connector, 5, a pinch clamp 6, a male

luer 8, a female luer 26, a 0.22 micron pore anti pyrogen filter 11, a non reopener

tubing clamp 13, a non-breathing cap 14 on a femal luer 9, an in-line check valve 16,

a pinch clamp 18, a break-off male luer cap and female luer 19, and a female luer 21 and tubing branches 3, 7, 10, 12, 15, 17, and 20. The replacement fluid container 1 is delivered to a patient treatment setting as a sealed sterile container with all terminals sealed. The replacement fluid container contains, as delivered, a concentrate solution sufficient to create a treatment batch of replacement fluid when water is added.

Concentrate may be added by means of the luer connector 21. In the deliverable to the treatment site, the tubing branch 20 may be sealed and cut after the concentrate is added. Water is added at the treatment site through connection to a water source via luer 19. The water is preferably metered to provide a predefined quantity. The 0.22 micron filter is sufficient to protect against contamination before water is added to the replacement fluid container 1. A sample of diluted replacement fluid may be drawn through the luer 19 before treatment. The check valve 16 prevents any contamination due to backflow from the sampling procedure. After water is added to the replacement fluid container 1, the luer 9 is disconnected from the male luer 8 and the male luer connector connected to the blood treatment system.

To supply suitable water that is substantially free of unwanted dissolved and undissolved materials, a combination of permanent and replaceable components may be provided at the treatment site. Fig. 13 illustrates such a set up in overview fashion. A pretreatment module 900 provides primary filtration from a raw water supply, for example tap water and feeds prefiltered water to a controller module 905 which provides various control functions, a pump, pressure detection and control, and permanent filtering capabilities which are not shown separately here. Water is metered by the control module into a consumable disposable module 910 which may provide deionization, adsorption filtration, microporous filtering, chemical

pretreatment, etc. and any other types of filtering that may require replacement of components. The purified water is finally conveyed to the replacement fluid container circuit 915 discussed with reference to Fig. 12.

- Referring to Fig. 14, pretreatment module 900 is shown in more detail.
- 5 A check valve 955 prevents backflow. An air vent 953 removes air from the primary supply and a sediment filter 951 (which may be replaceable) provides substantial filtering of solids.

Referring to Fig. 15, the control module 905 is shown in greater detail. A shutoff valve 1010 is provided for safety. Pressure indicators 1015 and 1025 may 10 be provided for monitoring the respective pressures in and out of a pump 1020. Feedback regulation may be provided to ensure that consistent metering is provided if the pump is relied upon for measuring the total quantity of water supplied to the replacement fluid container 1. A high intensity ultraviolet (UV) lamp 1030 provides a 15 sterilization mechanism. Preferably, the UV lamp 1030 is of such intensity and wavelength as to provide disintegration of chloramines. In a preferred embodiment, the lamp is characterized by a 245 nm wavelength and an output power of 750 mJ/cm<sup>2</sup> up to 1500 mJ/cm<sup>2</sup> which is sufficient to remove chloramines.

Referring to Fig. 16, the replaceable (disposable or remanufacturable) filter module 910 contains a first stage filter 1007 copper-zinc alloy which is used to 20 subject the water to a reduction/oxidation process to remove ions. This removes ions through a chemical reaction. An embodiment is KDF 85 media where about one pound is used for a flow rate of 150 ml./min water flow rate. A activated carbon filter 1005 follows which is a well-known adsorption type filter. Next three stages of strong acid cation 1011 and strong base anion 1009 filters follow in series. A sensor

1022 detects ion concentration by contact testing of the conductivity of the water. A signal is generated to indicate that this is the last allowed batch before replacement of the replaceable module 910. A mixed bed deionization filter 1030 is provided next and a safeguard conductivity test is provided with an audible alarm at 1025 as a back up safety measure. If the conductivity it detects is above a certain level, the pump 1020 may be shut off and an alarm sounded. This may come into play if an operator ignores the tester 1022 which may provide a visual signal or if the tester 1022 fails.

5 TP is a hydrophobic membrane air vent which allows air in an ultrafilter 1035 to be purged. The ultrafilter 1035 may be a microtubular filter such as used for dialysis. A 10 1.2 micron air vent may also be provided as shown at 1047.

Note the final conductivity sensor/alarm 1025 may control the pump, as noted. A controller 1090 may be connectable to the disposable filter module 910 and configured to stop the pump 1020. The trigger resistivity safety level to cut-off the pump 1020 may be 1 megaohm, but may be raised to 2 megohm to allow the use 15 of required temperature compensated resistivity probes (an FDA & AAMI requirement) This does allow use of low cost in-line resistivity probes in the disposable filter module 910.

The following is a procedure for using the above devices discussed with reference to Figs. 12-16.

- 20 1. Remove the dialysate concentrate tubing set 915 and remove the cap 14 from the tubing line 7 that contains the filter 11. (The 0.22 micron filter 11 provides additional protection from inadvertent contamination.)
2. Connect the water source to the concentrate bag luer connection 9.
3. Break the frangible luer connector 4 which connector is configured

to form a permanent seal on the side facing the Y-junction 5 when disconnected.

4. Add 3 liters of water into the concentrate bag using the purification plant through tubing branch 7 through luer connector 9.

5. Write on the bag label the date and time water was first added to the concentrate bag, to assist in ensuring that it is used within 24 hours.

6. Shake the replacement fluid container 1 well to mix.

7. Confirm solution conductivity prior to use. Remove the break-off cap 1 and draw sample from this branch 16. After removing the sample, clamp the line using the pinch clamp 18 provided.

10 8. (The following is normative according to a preferred embodiment and not limiting of the invention) Conductivity must be in the range 13.0 to 14.4 mS. Nominal conductivity for the dialysate solution is 13.7 mS at 25°C. If conductivity does not meet this specification do not use it. Verify that the results are accurate. If conductivity is high additional water may be added to bring it within specification. If 15 conductivity is low then the solution must be discarded.

9. Using the non re-opening clamp 13 provided, clamp the line that is connected to the water purification plant.

10. Using the clamp 6 is next clamped on the line that is connected to the dialysate bag1.

20 11. Disconnect the water source at the luer connection 26

12. Connect the bag of dialysate solution to the dialysis circuit at the connection 8. This leaves the filter 11 and permanent clamp 13 in place to protect the water supply source.

13. Unclamp the line going to the dialysate bag (red clamp), and

initiate treatment after verifying that dialysate will be used within 24 hours from when water was added.

Although the foregoing invention has, for the purposes of clarity and understanding, been described in some detail by way of illustration and example, it  
5 will be obvious that certain changes and modifications may be practiced that will still fall within the scope of the appended claims. For example, the devices and methods of each embodiment can be combined with or used in any of the other embodiments.

What is claimed is:

- 1        1. A method of administering a renal replacement therapy requiring an  
2        infusible fluid, comprising the steps of:
  - 3                sterile-filtering a source fluid whose sterility is not assured, whereby  
4                said infusible fluid is generated;
  - 5                flowing said infusible fluid into a sterile batch container;
  - 6                said steps of sterile-filtering and flowing including performing said  
7                steps at a location and time at which a patient is to be infused with said infusible fluid;  
8                and
  - 9                diluting a patient's blood with said infusible fluid from said sterile  
10          batch container during a treatment phase.
- 1        2. A method as in claim 1, wherein said steps of sterile-filtering and  
2        flowing including connecting a tubing set including said batch container to a supply  
3        of said source fluid.
- 1        3. A method as in claim 2, wherein said tubing set is disposable.
- 1        4. A method as in claim 1, wherein said step of sterile-filtering  
2        includes urging one of said source fluid and said infusible fluid through a filter by  
3        means of pressure developed by a pump.
- 1        5. A method as in claim 1, wherein said step of sterile-filtering  
2        includes urging one of said source fluid and said product through a filter by means of  
3        pressure developed by gravity.
- 1        6. A method as in claim 5, wherein:
  - 2                said step of sterile-filtering includes flowing said source fluid through  
3                a filter; and

4                   a flow capacity of said filter is less than a rate of consumption of said  
5                   infusible fluid required during said treatment phase.

1                   7. A method as in claim 6, wherein said step of sterile filtering includes  
2                   blocking air bubbles in said source fluid from flowing into said sterile batch container.

1                   8. A method as in claim 1, wherein at least one of said steps of sterile-  
2                   filtering and flowing includes automatically controlling at least one of a flow rate of  
3                   said infusible fluid and a rate of heating of said infusible fluid responsively to data  
4                   representing at least one of a treatment start time and a volume of said fluid infusible  
5                   fluid required for said treatment phase.

1                   9. A method as in claim 8, further comprising entering said start time,  
2                   said step of entering including scanning a data storage device attached to a component  
3                   employed during at least one of said sterile-filtering, flowing, and diluting.

1                   10. A method as in claim 9, wherein said component is one of a  
2                   consumable, a disposable container for a consumable, and a disposable fluid circuit.

1                   11. A method as in claim 1, further comprising heating said infusible  
2                   fluid and insulating said sterile batch container against loss of heat.

1                   12. A method as in claim 1, further comprising heating said infusible  
2                   fluid to a predetermined temperature required for said treatment phase, a rate of said  
3                   step of heating being substantially less than a heat rate that would be required to heat  
4                   said infusible fluid from room temperature to said predetermined temperature at a rate  
5                   of flow of said infusible fluid during said step of diluting.

1                   13. A method as in claim 1, wherein said step of sterile-filtering  
2                   includes pumping one of said source fluid and said infusible fluid across a filter

3       membrane at a rate controlled to maintain a pressure drop across said membrane  
4       within a predetermined range.

1           14. A method as in claim 1, wherein at least one of said steps of sterile-  
2       filtering and flowing includes automatically controlling at least one of a flow rate of  
3       said infusible fluid and a rate of heating of said infusible fluid responsively to at least  
4       one of a predefined quantity or a remaining quantity of said source fluid.

1           15. A method as in claim 1, further comprising priming, with said  
2       infusible fluid, at least one of a replacement fluid circuit, a waste circuit, and a blood  
3       circuit of a renal replacement apparatus to rid the same of gas, said step of priming  
4       including recirculating said infusible fluid through said sterile batch container.

1           16. A method as in claim 15, wherein said step of priming includes  
2       collecting gas in said sterile batch container and maintaining a temperature of said  
3       infusible fluid.

1           17. A method as in claim 16, wherein said step of priming includes  
2       insulating said sterile batch container.

1           18. A method as in claim 1, wherein said renal treatment portion  
2       includes at least one of hemofiltration and hemodiafiltration.

1           19. A method as in claim 1, wherein said renal treatment portion  
2       includes hemofiltration.

1           20. A method as in claim 19, wherein said tubing set is disposable.

1           21. A method as in claim 19, wherein said step of sterile-filtering  
2       includes urging one of said source fluid and said infusible fluid through a filter by  
3       means of pressure developed by a pump.

1               22. A method as in claim 19, wherein said step of sterile-filtering  
2     includes urging one of said source fluid and said product through a filter by means of  
3     pressure developed by gravity.

1               23. A method as in claim 22, wherein:  
2                said step of sterile-filtering includes flowing said source fluid through  
3     a filter; and  
4                a flow capacity of said filter is less than a rate of consumption of said  
5     infusible fluid required during said treatment phase.

1               24. A method of administering renal replacement therapy, comprising  
2     the steps of:  
3                at a location at which a patient is to be treated, sterile-filtering a source  
4     fluid;  
5                flowing a sterile replacement fluid resulting from said step of sterile-  
6     filtering into a batch container;  
7                a rate of said flowing being less than a rate of consumption of said  
8     sterile replacement fluid during a treatment time;  
9                heating said sterile replacement fluid to a temperature required for  
10    infusion by applying heat to at least one of a said source fluid and said sterile  
11    replacement fluid;  
12               maintaining said sterile replacement fluid at said temperature until a  
13    beginning of said treatment time.

1               25. A method as in claim 24, wherein said batch container is a part of a  
2     disposable fluid circuit.

1               26. A method as in claim 24, wherein said step of flowing includes  
2 pumping at least one of said source fluid and said sterile replacement fluid.

1               27. A method as in claim 24, wherein said step of flowing includes  
2 feeding said sterile replacement fluid by means of a gravity feed.

1               28. A method as in claim 27, wherein said step of sterile-filtering  
2 includes passing said source fluid through a filter whose capacity is such as to permit  
3 a maximum flow therethrough that is limited to a rate that is substantially less than a  
4 rate of consumption of said sterile replacement fluid during a treatment time.

1               29. A method as in claim 28, further comprising insulating batch  
2 container.

1               30. A method as in claim 29, wherein a rate of said step of heating is  
2 substantially less than a heat rate that would be required to heat said infusible fluid  
3 from room temperature to said temperature required for infusion at a rate of  
4 consumption during said treatment time.

1               31. A method as in claim 24, further comprising insulating batch  
2 container.

1               32. A method as in claim 24, wherein a rate of said step of heating is  
2 substantially less than a heat rate that would be required to heat said infusible fluid  
3 from room temperature to said temperature required for infusion at a rate of  
4 consumption during said treatment time.

1               33. A method as in claim 24, wherein said step of sterile-filtering is  
2 performed at a time immediately prior to said treatment time.

1               34. A method as in claim 24, wherein at least one of said steps of  
2 sterile-filtering and flowing includes automatically controlling at least one of a flow

3       rate of said sterile replacement fluid and a rate of said heating responsively to data  
4       representing at least one of a start of said treatment time and a volume of said sterile  
5       replacement fluid to be consumed for said renal replacement therapy.

1           35. A method of delivering an extracorporeal blood treatment requiring  
2       an infusible fluid, comprising the steps of:

3               insulating a batch fluid container;  
4               at a location where, and at time at which, a patient is to be  
5       administered said extracorporeal blood treatment, sterile-filtering a quantity of a  
6       source fluid and storing an infusible fluid resulting therefrom in said batch fluid  
7       container, said quantity being sufficient for said extracorporeal blood treatment;

8               heating at least one of said source fluid and said infusible fluid at a rate  
9       that is substantially less than a heat rate that would be required to heat said infusible  
10      fluid from room temperature to a temperature required for infusion at a rate of  
11      consumption during said extracorporeal blood treatment;

12               priming, with said infusible fluid, at least one of a replacement fluid  
13      circuit, a waste circuit, and a blood circuit of an extracorporeal blood treatment  
14      apparatus to rid the same of gas.

1           36. A method as in claim 35, wherein said step of sterile-filtering  
2       includes passing said source fluid through a filter, a flow capacity of said filter being  
3       less than a rate of consumption of said infusible fluid required during said  
4       extracorporeal blood treatment.

1           37. A method as in claim 36, wherein said filter is effective to remove  
2       air bubbles from said source fluid.

1                   38. A method as in claim 35, wherein said extracorporeal blood  
2 treatment includes a renal replacement therapy.

1                   39. A method as in claim 35, wherein said extracorporeal blood  
2 treatment includes one of hemofiltration and hemodiafiltration.

1                   40. A method as in claim 35, wherein said extracorporeal blood  
2 treatment includes hemofiltration.

1                   41. A method as in claim 35, wherein said step of priming includes  
2 recirculating said infusible fluid through said batch container, said batch container  
3 permitting a settling of gas bubbles out of said infusible fluid, said step of priming  
4 being such that said infusible fluid may remain sterile.

1                   42. A method of preparing an infusible fluid, comprising the steps of:  
2                   at a time and location of administration to a patient, sterile-filtering a  
3 fluid whose sterility is in question to yield a sterile infusible fluid;  
4                   heating said sterile infusible fluid to a temperature required for  
5 infusion;

6                   flowing said sterile infusible fluid into a batch container to permit it to  
7 be infused at a rate that is higher than a rate of said sterile-filtering.

1                   43. A method as in claim 42, further comprising, said batch container  
2 being part of a disposable sterile tubing set, priming said sterile tubing set with said  
3 sterile infusible fluid, said step of priming including recirculating said sterile infusible  
4 fluid through said batch container to permit bubbles to settle out.

1                   44. A method as in claim 42, wherein a rate of said step of heating is  
2 substantially less than a heat rate that would be required to heat said sterile infusible

3 fluid from room temperature to said temperature required for infusion at a rate of flow  
4 of said sterile infusible fluid during infusion thereof.

1 45. A tubing set for a renal replacement therapy requiring an infusible  
2 fluid, comprising:

3 a filter connectable to a fluid source to filter and thereby yield an  
4 infusible sterile fluid;

5 said filter being of a configuration to prevent pathogens from flowing  
6 across a membrane thereof;

7 a batch container connected to said filter to receive said infusible  
8 sterile fluid;

9 said tubing set being adapted for one-time use at a location and time at  
10 which a patient is to be infused with said infusible fluid; and

11 said batch container being provided with at least one connector to  
12 permit it to convey said infusible sterile fluid to a fluid circuit used in the performance  
13 of renal therapy at a rate that is independent of a rate permitted by said sterile-filter.

1 46. A set as in claim 45, further comprising a portion adapted to  
2 cooperate with a pump to convey said source fluid through said filter.

1 47. A set as in claim 45, wherein a flow capacity of said filter is less  
2 than a rate of consumption of said infusible fluid required during infusion of said  
3 patient.

1 48. A set as in claim 47, wherein said filter is effective to block air  
2 bubbles in said source fluid from flowing into said batch container.

1 49. A set as in claim 45, wherein said batch container is fitted with  
2 connectors to permit it to be connected temporarily with at least one of a replacement

3        fluid circuit, a waste circuit, and a blood circuit of blood treatment circuit, such that  
4        said infusible fluid can be recirculated through said batch container to rid said at least  
5        one of a replacement fluid circuit, a waste circuit, and a blood circuit of blood  
6        treatment circuit of gas by settling said gas out of said infusible fluid into said batch  
7        container.

1                50. A method as in claim 45, wherein said renal replacement therapy  
2        includes at least one of hemofiltration and hemodiafiltration.

1                51. A set as in claim 50, further comprising a portion adapted to  
2        cooperate with a pump to convey said source fluid through said filter.

1                52. A set as in claim 50, wherein a flow capacity of said filter is less  
2        than a rate of consumption of said infusible fluid required during infusion of said  
3        patient.

1                53. A set as in claim 52, wherein said filter is effective to block air  
2        bubbles in said source fluid from flowing into said batch container.

1                54. A set as in claim 50, wherein said batch container is fitted with  
2        connectors to permit it to be connected temporarily with at least one of a replacement  
3        fluid circuit, a waste circuit, and a blood circuit of blood treatment circuit, such that  
4        said infusible fluid can be recirculated through said batch container to rid said at least  
5        one of a replacement fluid circuit, a waste circuit, and a blood circuit of blood  
6        treatment circuit of gas by settling said gas out of said infusible fluid into said batch  
7        container.

1                55. A method as in claim 45, wherein said renal replacement therapy  
2        includes hemofiltration.

1               56. A set as in claim 55, further comprising a portion adapted to  
2   cooperate with a pump to convey said source fluid through said filter.

1               57. A set as in claim 55, wherein a flow capacity of said filter is less  
2   than a rate of consumption of said infusible fluid required during infusion of said  
3   patient.

1               58. A set as in claim 57, wherein said filter is effective to block air  
2   bubbles in said source fluid from flowing into said batch container.

1               59. A set as in claim 55, wherein said batch container is fitted with  
2   connectors to permit it to be connected temporarily with at least one of a replacement  
3   fluid circuit, a waste circuit, and a blood circuit of blood treatment circuit, such that  
4   said infusible fluid can be recirculated through said batch container to rid said at least  
5   one of a replacement fluid circuit, a waste circuit, and a blood circuit of blood  
6   treatment circuit of gas by settling said gas out of said infusible fluid into said batch  
7   container.

1               60. A tubing set for a renal replacement therapy requiring an infusible  
2   fluid, comprising:

3               a filter connectable to a fluid source to filter and thereby yield an  
4   infusible sterile fluid;

5               said filter being of a configuration to prevent pathogens from flowing  
6   across a membrane thereof and to block air bubbles;

7               a batch container connected to said filter to receive said infusible  
8   sterile fluid;

9               said tubing set being adapted for one-time use at a location and time at  
10   which a patient is to be infused with said infusible fluid; and

11                   said batch container being provided with at least one connector to  
12    permit it to convey said infusible sterile fluid to a fluid circuit used in the performance  
13    of renal therapy and also fitted with connections to permit recirculation of fluid  
14    through said fluid circuit to remove gas from said fluid circuit by permitting air to  
15    settle in said batch container.

1                   61. A set as in claim 60, further comprising a portion adapted to  
2    cooperate with a pump to convey said source fluid through said filter.

1                   62. A set as in claim 60, wherein a flow capacity of said filter is less  
2    than a rate of consumption of said infusible fluid required during infusion of said  
3    patient.

1                   63. A set as in claim 62, wherein said filter is effective to block air  
2    bubbles in said source fluid from flowing into said batch container.

1                   64. A set as in claim 60, wherein said batch container is fitted is  
2    provided with at least one connector to permit it to convey said infusible sterile fluid  
3    to a fluid circuit used in the performance of renal therapy at a rate that is independent  
4    of a rate permitted by said sterile-filter

1                   65. A device for generating an infusible fluid for administering a renal  
2    replacement therapy, comprising:

3                   a fluid circuit including a filter connectable to a source fluid supply  
4    and configured to sterilize said source fluid, whereby said infusible fluid is generated;  
5                   said fluid circuit including a sterile batch container connected to said  
6    fluid circuit to receive said infusible fluid from said filter;

7               said sterile batch container being connectable to a treatment device  
8       adapted to administer renal therapy and to draw said infusible fluid from said batch  
9       container and dilute a patient's blood with said infusible fluid;  
10              a controller configured to control a sterile-filtering process to generate  
11       said infusible fluid by permitting a flow of said source fluid through said filter and  
12       into said batch container;  
13              said controller being configured further to control at least one of a rate  
14       of filtering of said infusible fluid and a rate of heating of said infusible fluid  
15       responsively to data representing at least one of a start time of a renal replacement  
16       therapy and a volume of said fluid infusible fluid required for said renal replacement  
17       therapy.

1               66. A device as in claim 65, wherein said fluid circuit is a disposable  
2       tubing set.

1               67. A device as in claim 65, further comprising a pump engageable  
2       with said fluid circuit to urge at least one of said source fluid and said infusible fluid  
3       through said filter by means of pressure developed by said pump.

1               68. A device as in claim 65, wherein said source fluid is urged through  
2       said filter by gravity.

1               69. A device as in claim 68, wherein a flow capacity of said filter is  
2       less than a rate of consumption of said infusible fluid required during said renal  
3       therapy.

1               70. A device as in claim 65, wherein a media of said filter is of a type  
2       that prevents gas bubbles in said source fluid from flowing into said batch container.

1               71. A device as in claim 65, wherein said controller is configured to  
2   receive said start time by scanning a data storage device attached to a part of said fluid  
3   circuit.

1               72. A device as in claim 65, further comprising a heater configured to  
2   heat said infusible fluid in said batch container.

1               73. A device as in claim 73, wherein said heater is controlled by said  
2   controller to heat said infusible fluid to a predetermined temperature required for said  
3   renal therapy, a power capacity of said heater being substantially less than a heat rate  
4   that would be required to heat said infusible fluid from room temperature to said  
5   predetermined temperature at a rate of flow of said infusible fluid during said step of  
6   diluting.

1               74. A device as in claim 65, further comprising a pump engageable  
2   with said fluid circuit to urge at least one of said source fluid and said infusible fluid  
3   through said filter by means of pressure developed by said pump, said controller being  
4   configured to control a rate of said pumping across a filter membrane of said filter to  
5   maintain a pressure drop across said membrane within a predetermined range.

1               75. A device as in claim 65, wherein said controller is configured to  
2   control at least one of a rate of generation of said infusible fluid and a rate of heating  
3   of said infusible fluid responsively to at least one of a predefined quantity and a  
4   remaining quantity of said source fluid.

1               76. A device as in claim 65, wherein said batch container is fitted with  
2   connectors to permit it to be connected temporarily with at least one of a replacement  
3   fluid circuit, a waste circuit, and a blood circuit of renal therapy device such that said  
4   infusible fluid can be recirculated through said batch container to rid said at least one

5 of a replacement fluid circuit, a waste circuit, and a blood circuit of blood treatment  
6 circuit of gas by settling said gas out of said infusible fluid into said batch container.

1           77. A device as in claim 76, wherein said controller is configured to  
2 maintain a temperature of said infusible fluid during a recirculation thereof through  
3 said renal therapy device.

1           78. A device as in claim 77, further comprising an insulating envelope  
2 configured to insulate said batch container.

1           79. A device as in claim 65, wherein said treatment device is adapted  
2 to administer at least one of hemofiltration and hemodiafiltration.

1           80. A device as in claim 65, wherein treatment device is adapted to  
2 administer hemofiltration.

1           81. A device as in claim 80, wherein said fluid circuit is a disposable  
2 tubing set.

1           82. A device as in claim 80, further comprising a pump engageable  
2 with said fluid circuit to urge at least one of said source fluid and said infusible fluid  
3 through said filter by means of pressure developed by said pump.

1           83. A device as in claim 80, wherein said source fluid is urged through  
2 said filter by gravity.

1           84. A device as in claim 83, wherein a flow capacity of said filter is  
2 less than a rate of consumption of said infusible fluid required during said renal  
3 therapy.

1           85. A device for generating, at a treatment location, an infusible fluid  
2 for use in a renal replacement therapy to be performed at said location, the device  
3 comprising:

4                   a fluid circuit including a filter connected between a first connector  
5                   connectable to a source fluid supply and a batch container for receiving an infusible  
6                   fluid generated by sterile-filtering said source fluid with said filter;  
7                   said sterile batch container having fixtures adapted for connecting to a  
8                   renal therapy device which draws said infusible fluid from said batch container and  
9                   dilutes a patient's blood with said infusible fluid;  
10                  a heater configured to heat contents of said batch container;  
11                  a rate of flow permitted by said filter being less than a maximum rate  
12                  of draw by said renal therapy device;  
13                  an insulating envelope configured to insulate said batch container.

1                 86. A device as in claim 85, wherein said fluid circuit is a disposable  
2                 tubing set.

1                 87. A device as in claim 85, further comprising a pump engageable  
2                 with said fluid circuit to urge at least one of said source fluid and said infusible fluid  
3                 through said filter by means of pressure developed by said pump.

1                 88. A device as in claim 85, wherein said source fluid is urged through  
2                 said filter by gravity.

1                 89. A device as in claim 85, further comprising:  
2                 a controller configured to control a sterile-filtering process to generate  
3                 said infusible fluid by permitting a flow of said source fluid through said filter and  
4                 into said batch container;

5                 said controller being configured further to control at least one of a rate  
6                 of filtering of said infusible fluid and a rate of heating of said infusible fluid by said  
7                 heater responsively to data representing at least one of a start time of a renal

8 replacement therapy and a volume of said fluid infusible fluid required for said renal  
9 replacement therapy.

1 90. A device for delivering an extracorporeal blood treatment requiring  
2 an infusible fluid, comprising:

3 an insulated batch container;  
4 a filter connectable between said batch container and a source fluid;  
5 a fluid circuit configured to convey sterilized fluid from said filter to  
6 said batch container;

7 a heater configured to heat said batch container contents at a rate that is  
8 substantially less than a heat rate that would be required to heat said sterilized fluid  
9 from room temperature to a temperature required for infusion at a rate of consumption  
10 during said extracorporeal blood treatment;

11 said batch container being adapted for priming, with said sterilized  
12 fluid, at least one of a replacement fluid circuit, a waste circuit, and a blood circuit of  
13 an extracorporeal blood treatment apparatus to rid the same of gas by recirculating  
14 said sterilized fluid through said batch container and permitting gas to settle in said  
15 batch container.

1 91. A device as in claim 90, wherein a flow capacity of said filter is  
2 less than a rate of consumption of said infusible fluid required during said  
3 extracorporeal blood treatment.

1 92. A device as in claim 91, wherein said filter is effective to remove  
2 air bubbles from said source fluid.

1 93. A device as in claim 90, wherein said extracorporeal blood  
2 treatment includes a renal replacement therapy.

1               94. A device as in claim 90, wherein said extracorporeal blood  
2 treatment includes one of hemofiltration and hemodiafiltration.

1               95. A device as in claim 90, wherein said extracorporeal blood  
2 treatment includes hemofiltration.

3               96. A device for preparing replacement fluid for an extracorporeal  
4 blood treatment, comprising:

5               a replaceable fluid circuit including a sealed presterilized replacement  
6 fluid container containing a replacement fluid concentrate, a microporous filter, and a  
7 port which allows diluting water to be added to said replacement fluid concentrate  
8 only by passing water through said microporous filter;

9               a water treatment plant connectable to said replaceable fluid circuit for  
10 supplying water, said water treatment plant including a permanent component  
11 including a metering pump and a replaceable filter component configured to  
12 decontaminate water provided to the plant from a source.

13               97. A device for preparing replacement fluid for an extracorporeal  
14 blood treatment, comprising:

15               a replaceable fluid circuit including a sealed presterilized replacement  
16 fluid container containing a replacement fluid concentrate, a microporous filter, and a  
17 port which allows diluting water to be added to said replacement fluid concentrate  
18 only by passing water through said microporous filter;

19               said replacement fluid container having said microporous filter  
20 arranged in inline fashion on a tubing branch connected thereto and disconnectable  
21 therefrom.

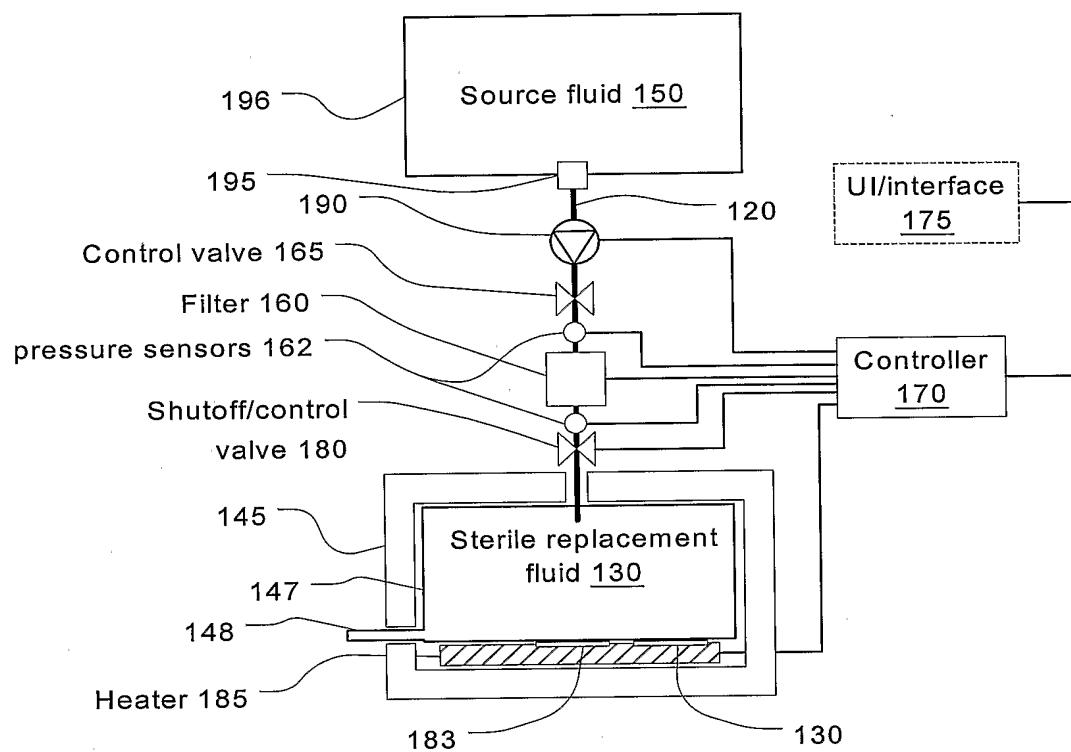
22            98. A water treatment plant for preparing replacement fluid for use in  
23        extracorporeal blood treatment, said plant including a strong acid cation followed by  
24        strong base anion to reduce colloidal aluminum (Alum) to soluble aluminum to aid in  
25        aluminum removal.

26            99. A water treatment plant for preparing replacement fluid for use in  
27        extracorporeal blood treatment, said plant including a resistivity monitor that is  
28        configured to shut a pump down when resistivity falls below a predetermined  
29        conductivity.

30            100. A plant as in claim 99, wherein said predetermined conductivity is  
31        about 2 megohms.

32            101. A water treatment plant for preparing replacement fluid for use in  
33        extracorporeal blood treatment, said plant including an ultraviolet lamp of such  
34        intensity and wavelength as to provide disintegration of chloramines.

35            102. A plant as in claim 101 in which said lamp is characterized by a  
36        245 nm wavelength and an output power of 750 mJ/cm<sup>2</sup> up to 1500 mJ/cm<sup>2</sup>.



**Fig. 1**

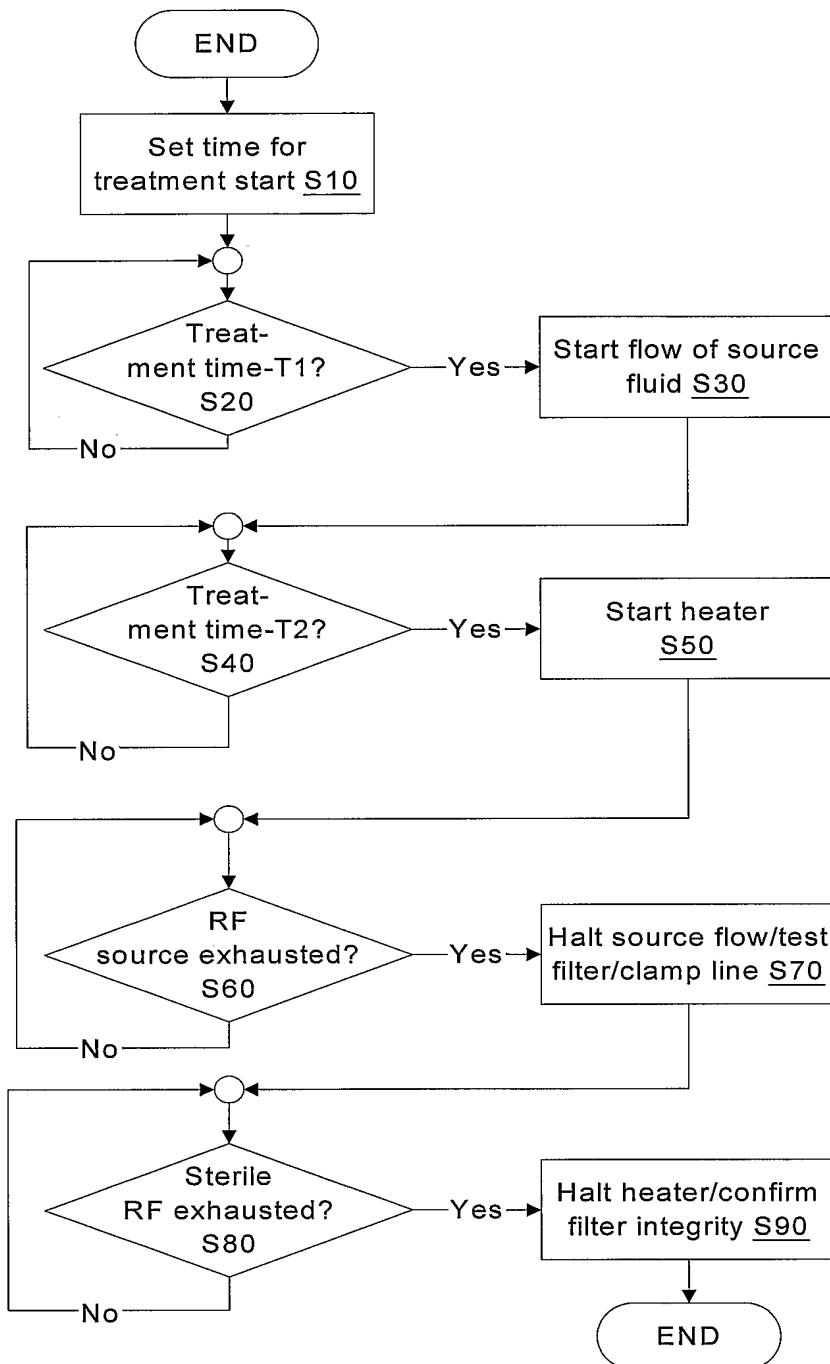
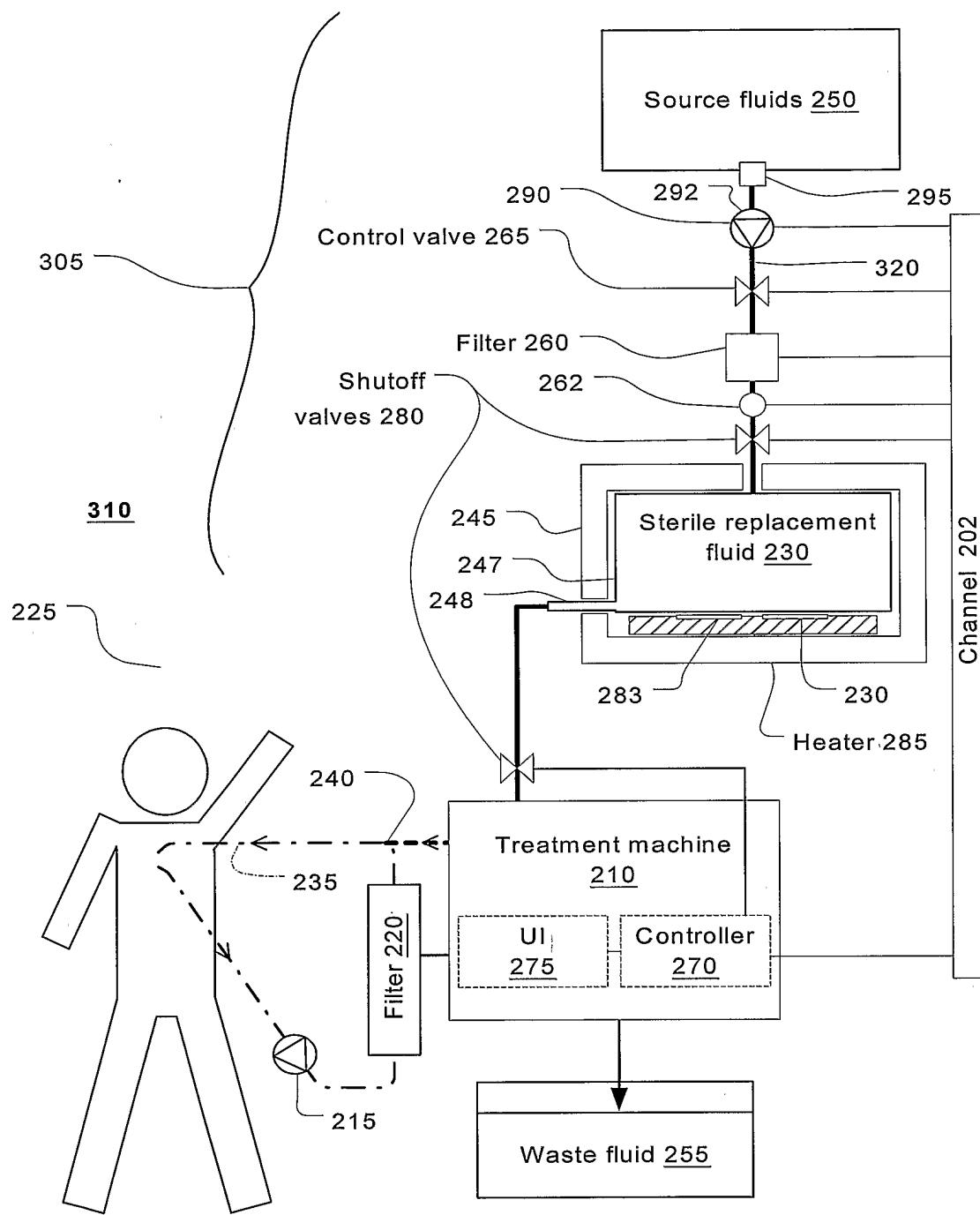
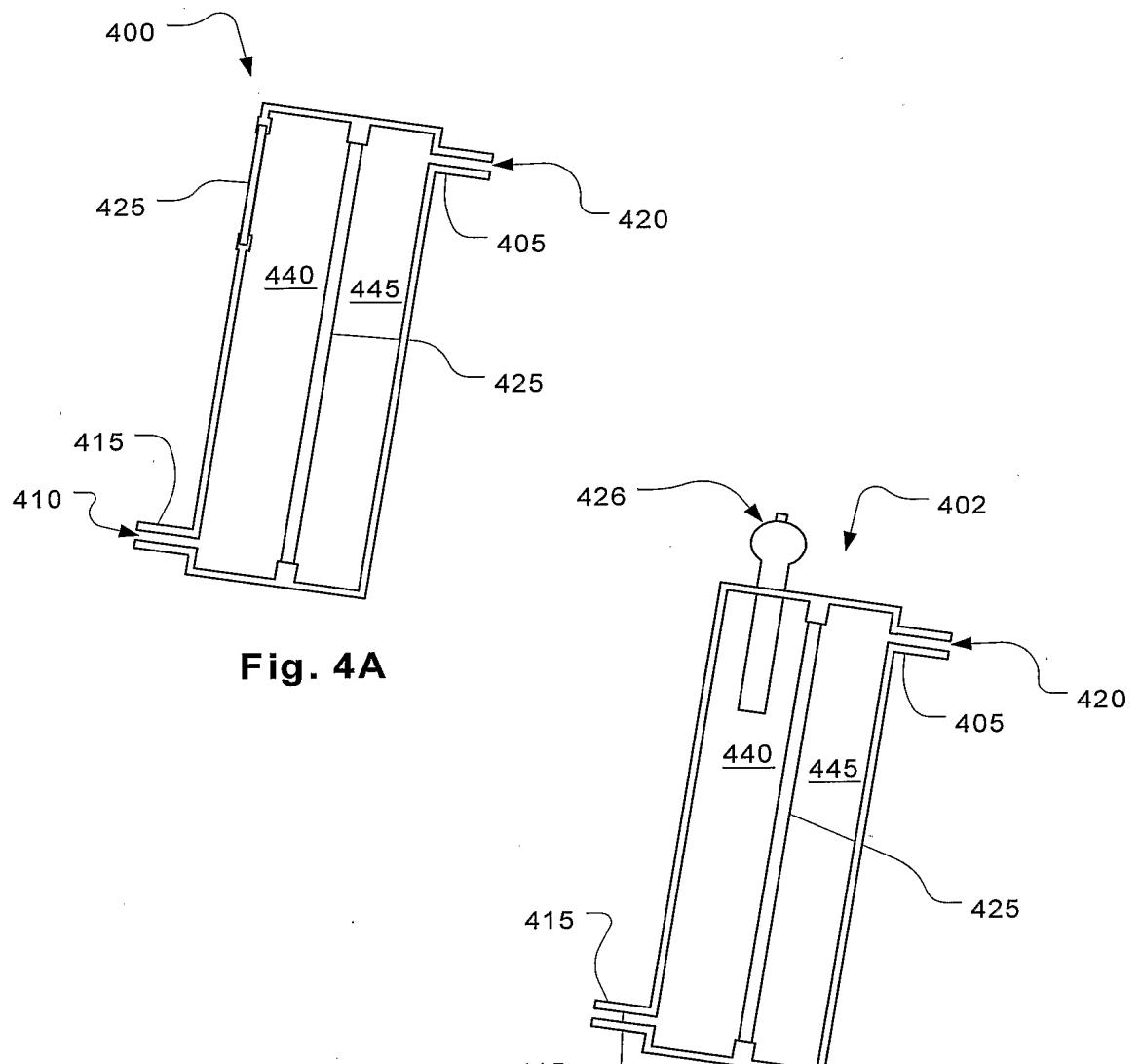
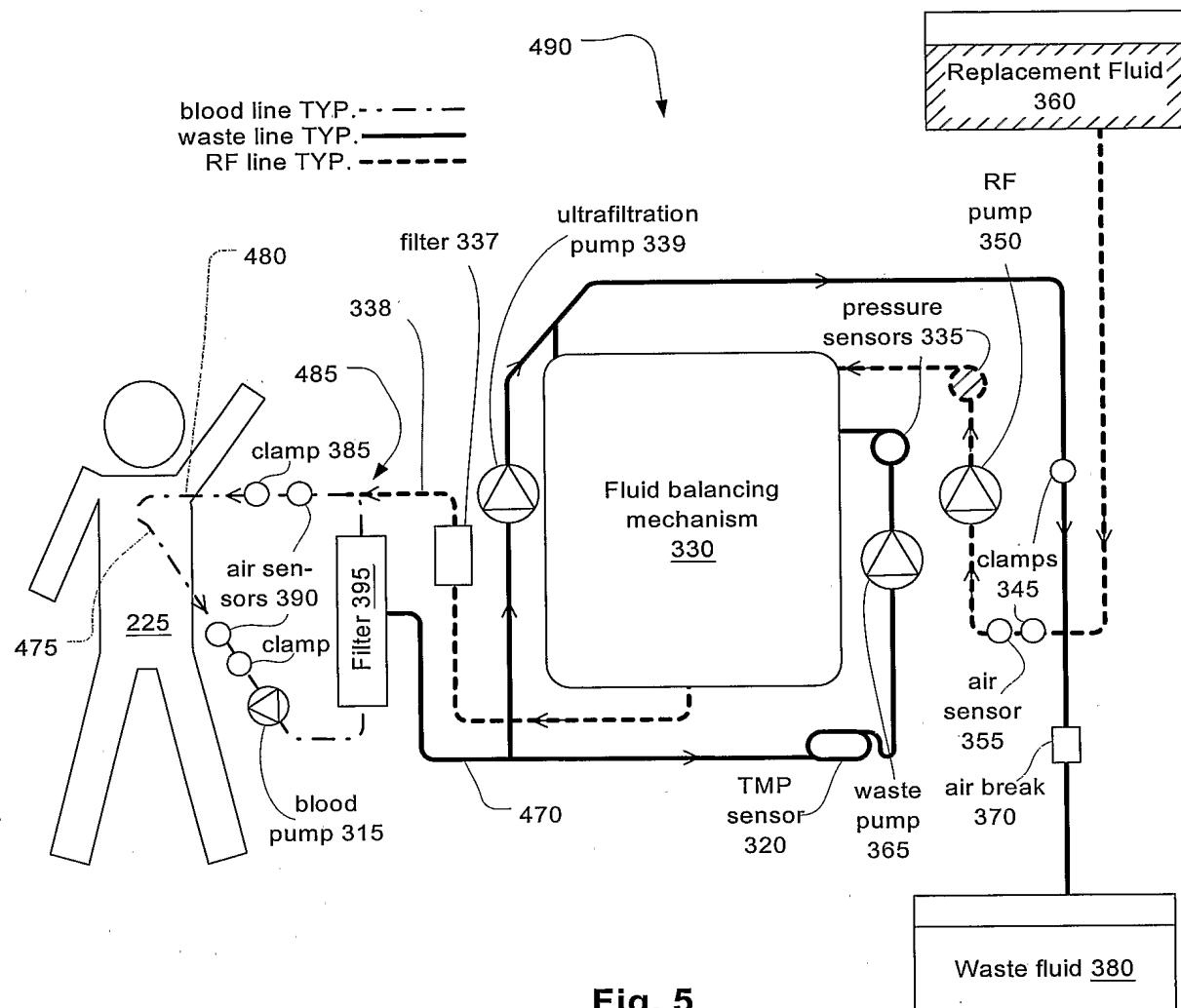


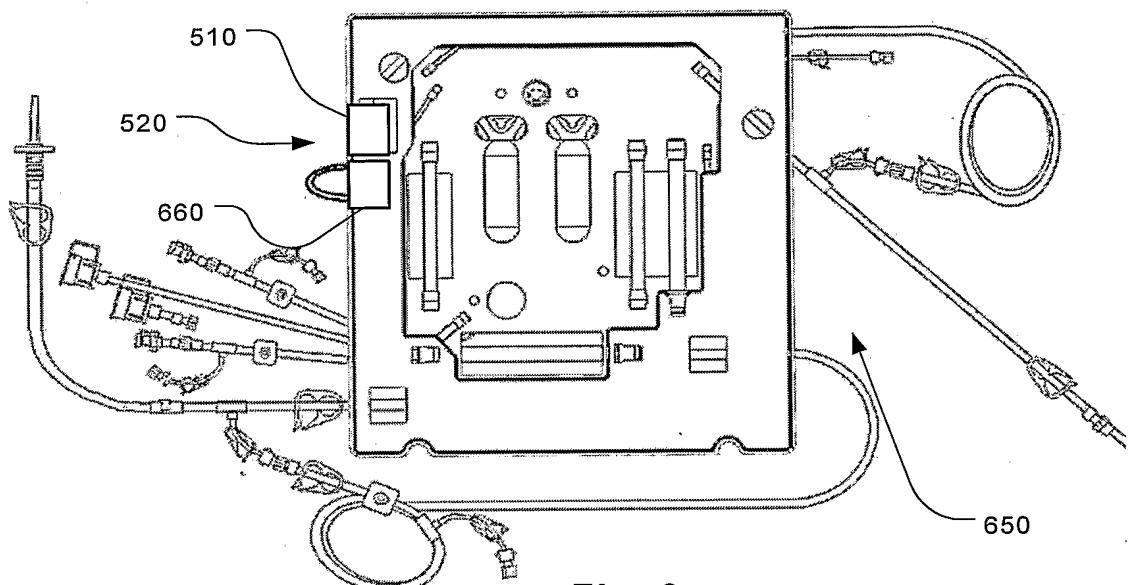
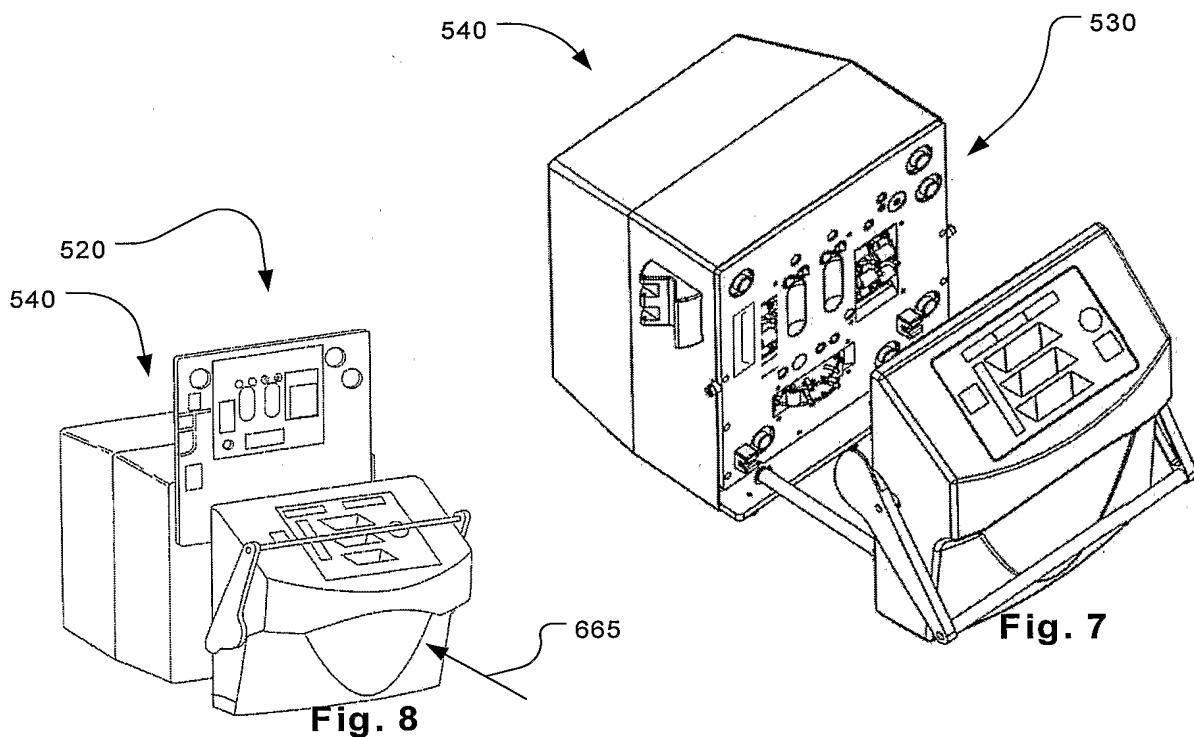
Fig. 2

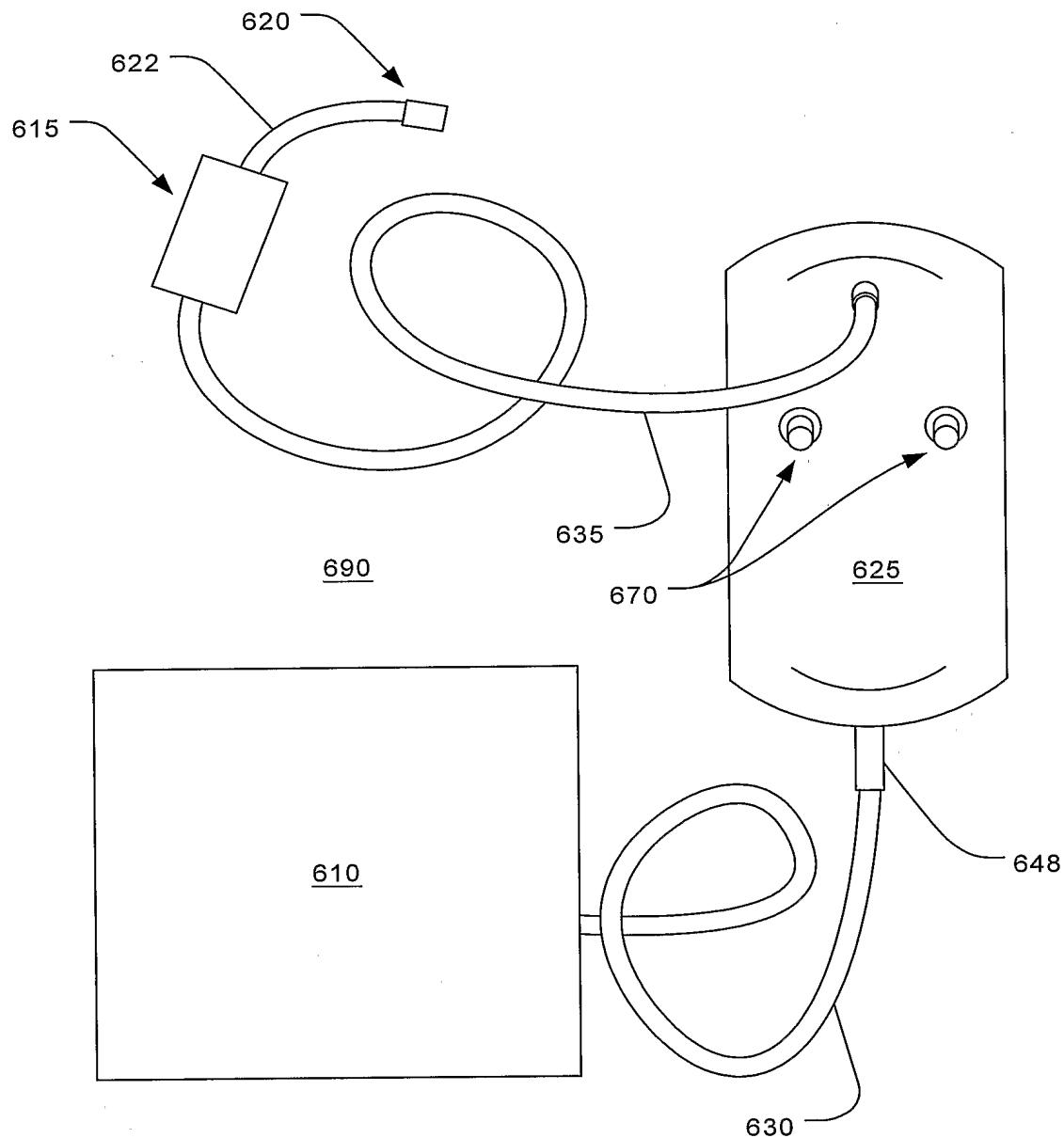


**Fig. 3**

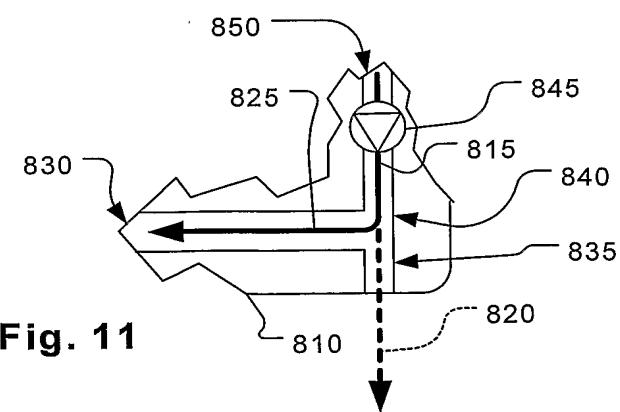
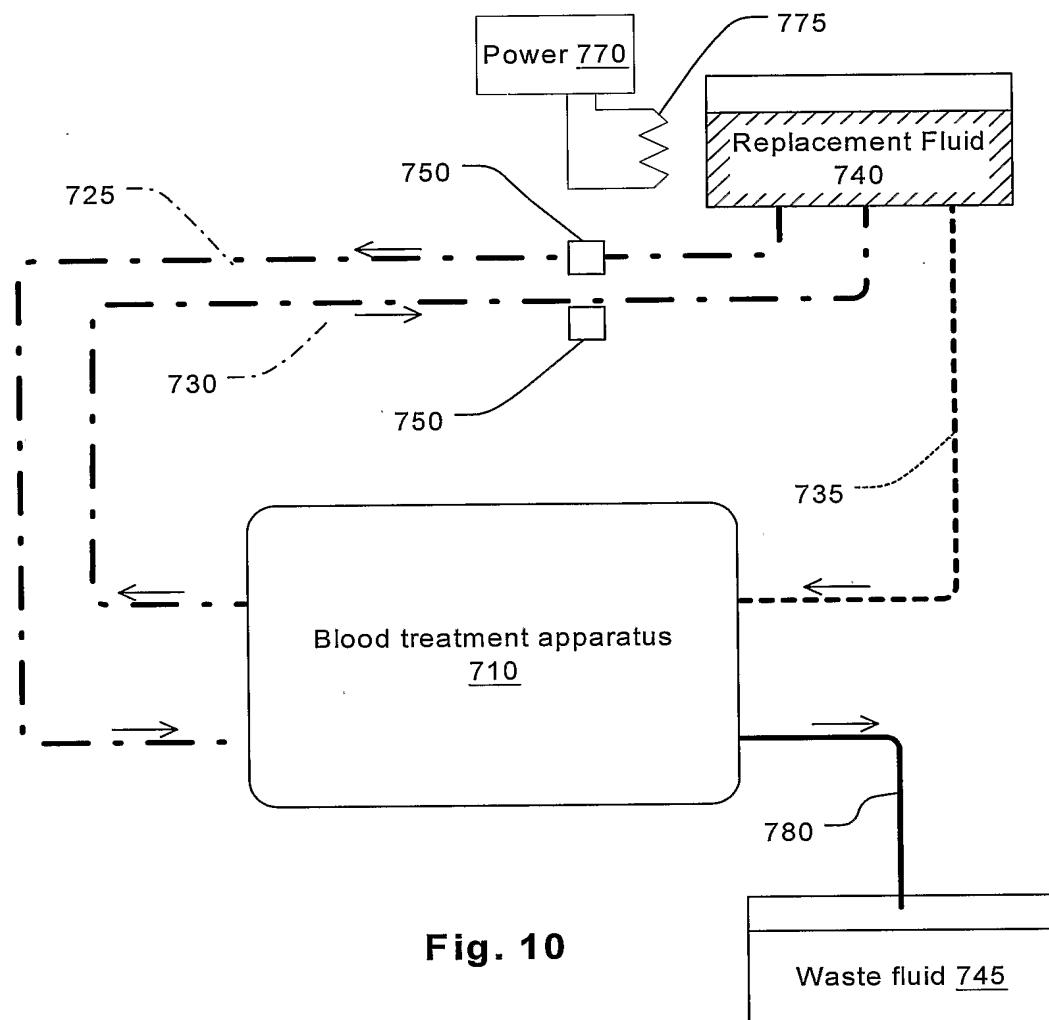


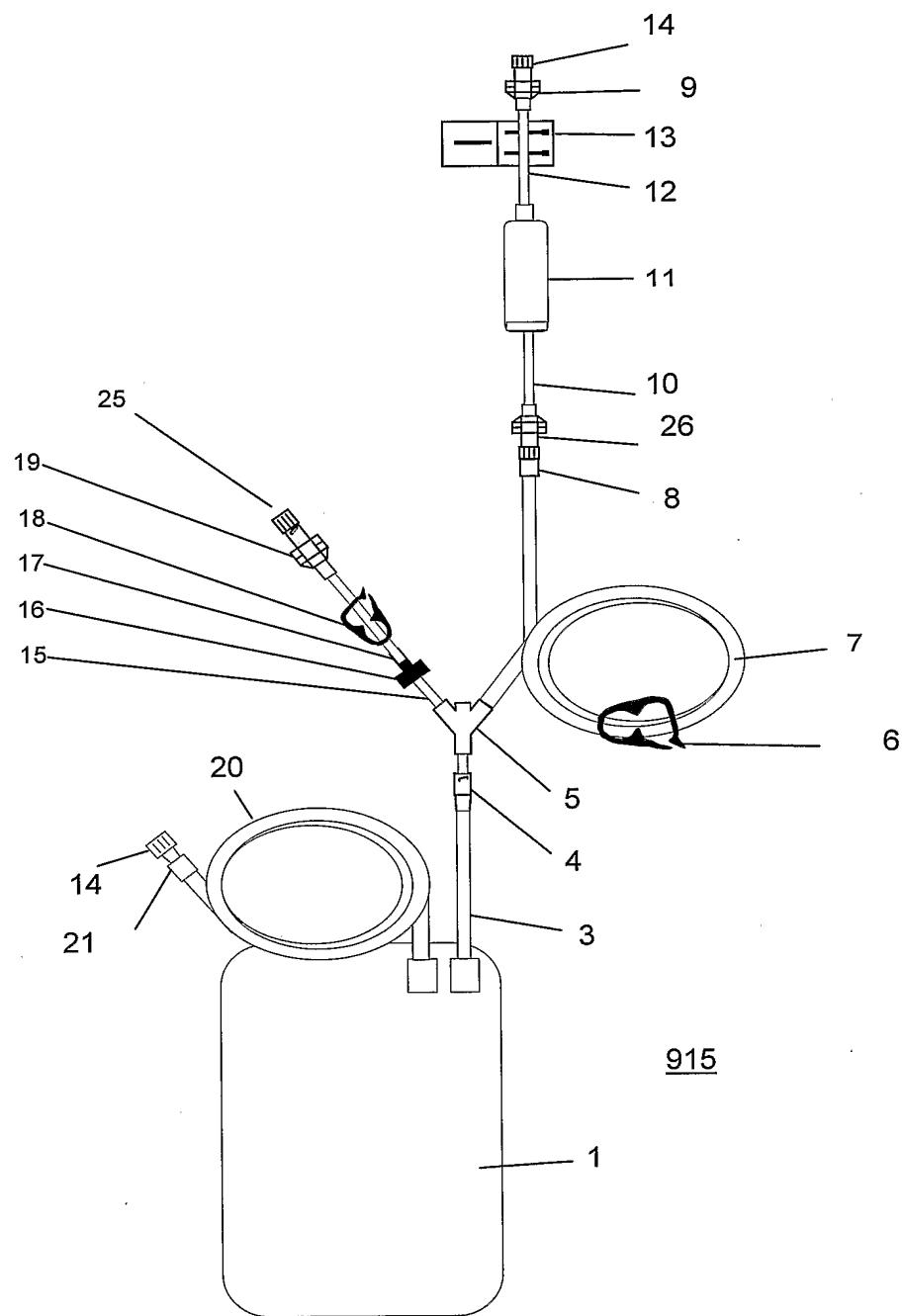
**Fig. 5**

**Fig. 6****Fig. 7****Fig. 8**

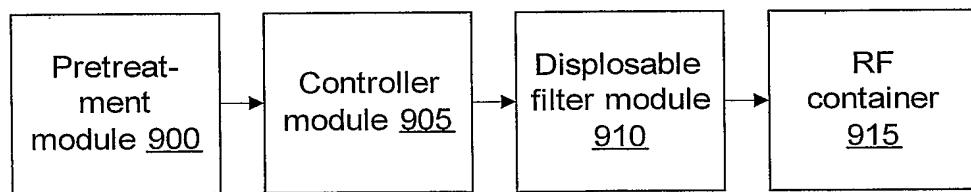


**Fig. 9**

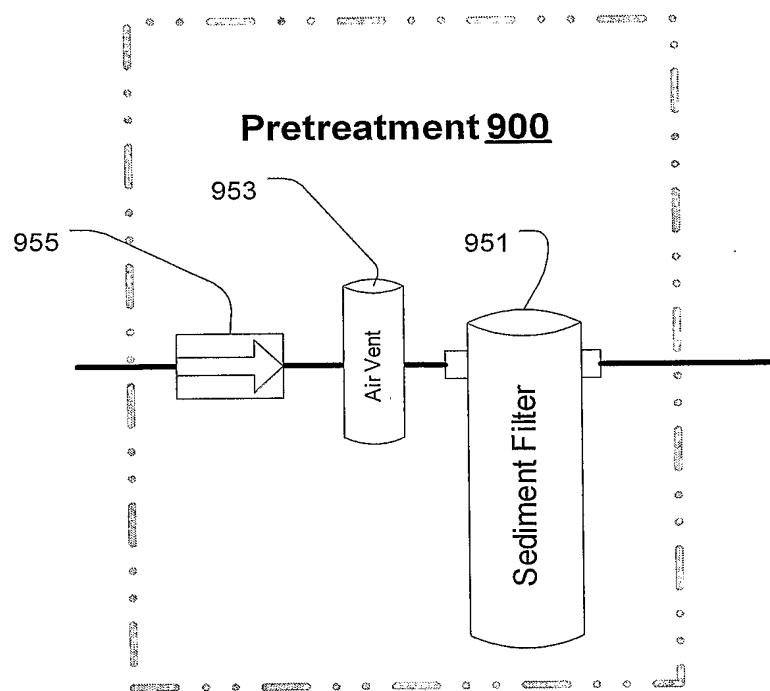




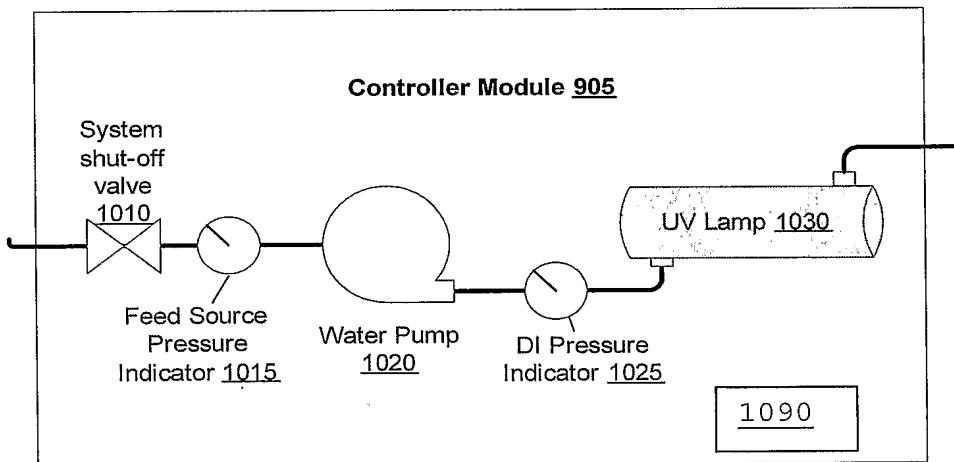
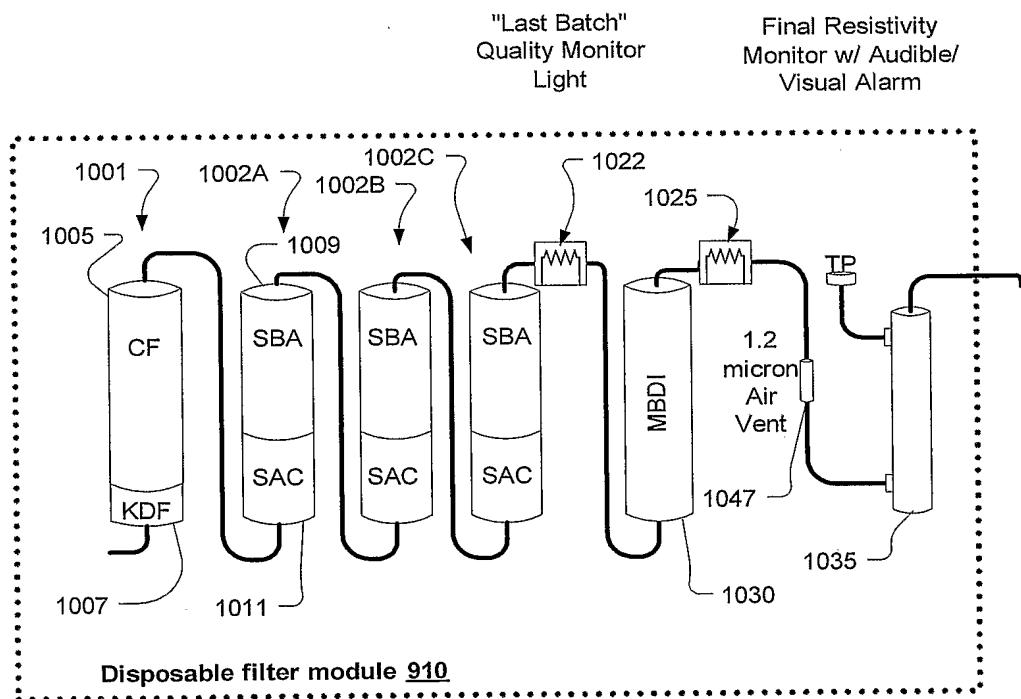
**Fig. 12**



**Fig. 13**



**Fig. 14**

**Fig. 15****Fig. 16**